

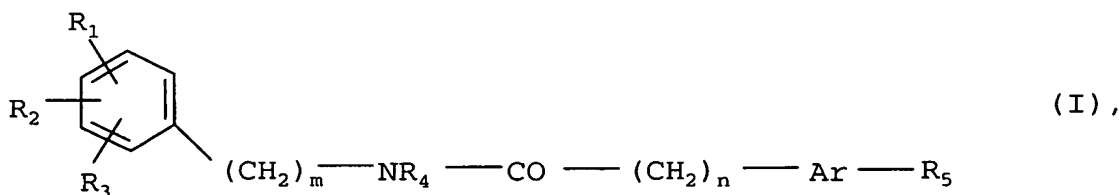
Please cancel claims 9 and 10.

Please add the following new claims:

-
11. -- The compound according to claim 1 wherein said carboxy groups are converted into a carboxy group *in vivo* or by a group which is negatively charged under physiological conditions.
12. The compound according to claim 1 wherein said amino and imino groups are replaced by a group that may be cleaved *in vivo*.
13. A method of treating a patient in need of a pharmaceutical composition having an antithrombotic activity or factor Xa inhibiting activity by administering to said patient a therapeutically effective amount of a component according to claim 6.
14. Pharmaceutical compositions containing a compound according to a salt of claim 6 optionally together with one or more inert carriers and/or diluents.--
-

AMENDED CLAIMS MARKED TO SHOW CHANGES MADE

1. (Amended) A Carboxylic acid amides compound of the following general formula



wherein

one of the groups m or n denotes the number 0 and
the other group m or n denotes the number 1,

Ar denotes a phenylene or naphthylene group optionally substituted by a fluorine, chlorine or bromine atom, by a trifluoromethyl, C₁₋₃-alkyl, hydroxy, C₁₋₃-alkoxy, phenyl-C₁₋₃-alkoxy, amino, C₁₋₃-alkylamino or di-(C₁₋₃-alkyl)-amino group, whilst the said phenylene group may be optionally substituted by a second another fluorine, chlorine or bromine atom or by another C₁₋₃-alkyl group,

a thienylene, thiazolylene, pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted in the carbon skeleton by a C₁₋₃-alkyl group,

R₁ denotes a C₁₋₃-alkyl group optionally substituted by an amino, C₁₋₃-alkylamino, di-(C₁₋₃-alkyl)-amino, phenyl, naphthyl, heteroaryl or 4- to 7-membered cycloalkyleneimino group,

a C₃₋₇-cycloalkyl group which is substituted in the 1 position by a 5- to 7-membered cycloalkyleneiminocarbonyl group,

an amino, C₁₋₅-alkylamino, C₅₋₇-cycloalkylamino or phenyl-C₁₋₃-alkylamino group which may in each case be substituted at the amino-nitrogen atom by a benzoyl or phenylsulphonyl group or by a C₁₋₃-alkyl or C₁₋₃-alkylcarbonyl group optionally substituted in the C₁₋₃-alkyl moiety by a carboxy group,

a 4- to 7-membered cycloalkyleneiminocarbonyl or cycloalkyleneiminosulphonyl group optionally substituted by a C₁₋₃-alkyl group,

an aminosulphonyl group optionally substituted by one or two C₁₋₃-alkyl groups, a phenyl group optionally substituted by a fluorine, chlorine or bromine atom, by a trifluoromethyl, aminosulphonyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group, which may additionally be substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group,

a C₁₋₃-alkoxy, phenyl-C₁₋₃-alkoxy, heteroaryloxy or heteroaryloxy-C₁₋₃-alkoxy group wherein the alkoxy moiety may be substituted in the 2 or 3 position in each case by an amino, C₁₋₃-alkylamino or di-(C₁₋₃-alkyl)-amino group,

a C₃₋₇-cycloalkoxy group, wherein ~~whilst~~ the methylene group in the 3 or 4 position in a C₅₋₇-cycloalkoxy group may be replaced by an -NH group, ~~whilst~~ and the said -NH group may be optionally substituted

by a C₁₋₃-alkyl group which may be substituted in the 2 or 3 position by an amino, C₁₋₃-alkylamino or di-(C₁₋₃-alkyl)-amino group, by a C₁₋₃-alkylcarbonyl, arylcarbonyl or arylsulphonyl group or

by an aminocarbonyl, C₁₋₃-alkylaminocarbonyl or di-(C₁₋₃-alkyl)-aminocarbonyl group, wherein in each case the oxygen atom of the carbonyl group is replaced by an imino group,

R₂ denotes a hydrogen, fluorine, chlorine or bromine atom, a C₁₋₃-alkyl, hydroxy or C₁₋₃-alkoxy group,

R₃ denotes a hydrogen atom or a C₁₋₃-alkyl group,

R₄ denotes a hydrogen atom or a C₁₋₃-alkyl group optionally substituted by a carboxy group and

R₅ denotes a cyano group or an amidino group optionally substituted by one or two C₁₋₃-alkyl groups, ~~whilst said by the above mentioned~~ heteroaryl groups consisting of ~~is meant~~ a 5-membered heteroaryl group optionally substituted by a C₁₋₃-alkyl group which contains, in the heteroaromatic moiety,

an imino group optionally substituted by a C₁₋₃-alkyl group, or an oxygen or sulphur atom,

an imino group optionally substituted by a C₁₋₃-alkyl group and an oxygen, sulphur or nitrogen atom,

an imino group optionally substituted by a C₁₋₃-alkyl group and two nitrogen atoms or

an oxygen or sulphur atom and two nitrogen atoms,

or a 6-membered heteroarylene group optionally substituted by a C₁₋₃-alkyl group which contains one or two nitrogen atoms in the heteroaromatic moiety,

~~the carboxy groups mentioned in the definition of the abovementioned groups may be replaced by a group which may be converted into a carboxy group *in vivo* or by a group which is negatively charged under physiological conditions or~~

~~The amino and imino groups in the definition of the aforementioned groups are replaced by a group which may be cleaved *in vivo*~~

the an isomers ~~and~~ or salts thereof.

2. (amended) The Ccompounds of ~~general~~ formula I according to claim 1 wherein

one of the groups m or n denotes the number 0 and
the other group m or n denotes the number 1,

Ar denotes a phenylene group optionally substituted by a fluorine, chlorine or bromine atom or by a methyl, hydroxy, methoxy or benzyloxy group, which may be substituted by another methyl group,

R₁ denotes a phenyl group optionally substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, aminosulphonyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group, which may additionally be substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group,

a methyl group substituted by a dimethylamino, pyrrolidino or imidazolyl group, wherein the imidazolyl moiety may be substituted by a methyl group,

an amino, C₁₋₅-alkylamino, cyclopentylamino or benzylamino group which may be substituted at the amino-nitrogen atom by a carboxy-C₁₋₂-alkyl, C₁₋₃-alkoxycarbonyl-C₁₋₂-alkyl, carboxy-C₁₋₂-alkylcarbonyl or C₁₋₃-alkoxycarbonyl-C₁₋₂-alkylcarbonyl group,

a benzoylamino or phenylsulphonylamino group,

a cyclopropyl group which is substituted in the 1 position by a 5- to 7-membered cycloalkyleneiminocarbonyl group,

an optionally methyl-substituted pyrrolidinocarbonyl, piperidinocarbonyl, pyrrolidinosulphonyl or piperidinosulphonyl group,

a C₁₋₃-alkoxy group wherein the alkoxy moiety in the 2 or 3 position may be substituted in each case by an amino, C₁₋₃-alkylamino or di-(C₁₋₃-alkyl)-amino group,

a phenyl-C₁₋₃-alkoxy or pyridinyloxy group,

a C₅₋₇-cycloalkoxy group wherein the methylene group in the 3 or 4 position may be replaced by an -NH group, ~~whilst the~~ said -NH group may be substituted

by a C₁₋₃-alkyl or C₂₋₃-alkanoyl group,

by a C₂₋₃-alkanoyl or aminocarbonyl group wherein in each case the oxygen atom of the carbonyl group is replaced by an imino group,

R₂ denotes a hydrogen, fluorine, chlorine or bromine atom, a methyl, hydroxy or methoxy group,

R₃ denotes a hydrogen atom or a methyl group,

R₄ denotes a hydrogen atom or a methyl or ethyl group optionally substituted by a carboxy or C₁₋₃-alkoxycarbonyl group and

R₅ denotes a cyano group or an amidino group optionally substituted by a C₁₋₆-alkoxycarbonyl or benzoyl group,

~~the~~ or an isomers or salts thereof.

3. (amended) The ~~C~~compounds of ~~general~~ formula I according to claim 1, wherein

one of the groups m or n denotes the number 0 and
the other group m or n denotes the number 1,

Ar denotes a phenylene group optionally substituted by a methyl, hydroxy, methoxy or benzyloxy group,

R₁ denotes a phenyl group optionally substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, aminosulphonyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group, which may additionally be substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group,

a cyclopropyl group which is substituted in the 1 position by a 5- to 7-membered cycloalkyleneiminocarbonyl group, or a 4- to 7-membered cycloalkyleneiminocarbonyl group,

an optionally methyl-substituted pyrrolidinocarbonyl, piperidinocarbonyl or pyrrolidinosulphonyl group,

R₂ denotes a hydrogen, fluorine, chlorine or bromine atom or a methyl group,

R₃ denotes a hydrogen atom or a methyl group,

R₄ denotes a hydrogen atom or a methyl or ethyl group substituted by a carboxy, methoxycarbonyl or ethoxycarbonyl group and

R₅ denotes an amidino group optionally substituted by a C₁₋₆-alkoxycarbonyl or benzoyl group,

~~or an~~ the isomers thereof and ~~or~~ the salts thereof.

4. (amended) A compound of the ~~The following compounds of general formula I~~
according to claim 1 selected from the following compounds:

(a) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(b) 2-(2-benzyloxy-5-carbamimidoyl-phenyl)-N-(2-ethoxycarbonyl-ethyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(c) 2-(2-hydroxy-5-carbamimidoyl-phenyl)-N-(2-ethoxycarbonyl-ethyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(d) 2-(2-hydroxy-5-carbamimidoyl-phenyl)-N-(2-carboxy-ethyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(e) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(piperidin-1-yl-carbonyl)-phenyl]-acetamide and

(f) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(2-aminosulphonyl-phenyl)-phenyl]-acetamide,

wherein the amidino group may additionally be substituted by a C₁₋₆-alkoxycarbonyl or benzoyl group, and the salts thereof.

5. (amended) A compound of formula 1 according to claim 1 as follows: 2-(5-Carbamidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide and the salts thereof.

6. (amended) A pharmaceutical composition comprising a compound according to claim 1 or a pPhysiologically acceptable salts thereof according to claims 1 to 5 wherein R₅ denotes ~~one of the said~~ amidino groups ~~mentioned in claims 1 to 5.~~

7. (amended) Pharmaceutical compositions containing a compound according to at least one of claims 1 to 5, wherein R_5 denotes one of the said amidino groups mentioned in claims 1 to 5, or a salt according to claim 6 optionally together with one or more inert carriers and/or diluents.

8. (amended) A method of treating a patient in need of a pharmaceutical composition having an antithrombotic activity or factor Xa inhibiting activity by administering to said patient a therapeutically effective amount of a component according to Use of a compound according to at least one of claims 1 to 5, wherein R_5 denotes one of the said amidino groups mentioned in claims 1 to 5, or a salt according to claim 6, for preparing a pharmaceutical composition having an antithrombotic activity.

11. (Added) The compound according to claim 1 wherein said carboxy groups are converted into a carboxy group *in vivo* or by a group which is negatively charged under physiological conditions.

12. (Added) The compound according to claim 1 wherein said amino and imino groups are replaced by a group that may be cleaved *in vivo*.

13. (Added) A method of treating a patient in need of a pharmaceutical composition having an antithrombotic activity or factor Xa inhibiting activity by administering to said patient a therapeutically effective amount of a component according to claim 6.

14. (Added) Pharmaceutical compositions containing a compound according to a salt of claim 6 optionally together with one or more inert carriers and/or diluents.--

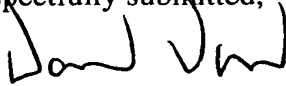
REMARKS

The claims have been amended to be more in conformance with standard U.S. practice. Claims 11 and 12 have been added, support being found in the original claim 1 and at page 6, lines 14-22 of the specification. Claim 7 has been redrafted as amended claim 7 and added Claim 14. The "Use" Claim 8 has been redrafted as a proper method Claim 8 and added Claim 13. There being no issues of new matter entry of these claims is respectfully requested.

Permission is hereby given to charge any additional fees to account number 02-2955.

If any points remain at issue that can best be resolved by way of telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,



David A. Dow
Attorney for Applicant(s)
Reg. No. 46,124

Patent Department
Boehringer Ingelheim Corp.
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877
Tel.: (203) 791-6214
Docket No.: 5/1266

"EXPRESS MAIL" LABEL NO.: EV 060 417 006 US
DEPOSIT DATE: February 6, 2002

I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE "EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE UNDER 37 CFR 1.10 ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE BOX PCT, ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20531.

By: 

David A. Dow
Reg. No. 46,124